REMARKS/ARGUMENTS

Applicants have amended the specification to rectify the incorrect "SEQ ID.:1" on page 11.

Applicants have amended the specification to capitalize trademarks.

No new matter has been added by way of these amendments.

Rejection Under 35 U.S.C. 112, First Paragraph

New Matter Rejection

The Office has rejected claims 17 and 18 as allegedly containing new matter for use of the phrase "after exposure to transplant therapy". These claims have been amended to recite "post-transplantation", rendering this rejection moot. However, Applicants note that transplant therapy (e.g, with an immunosuppressant) begins either directly before transplant, during transplant, or immediately after transplant. Moreover, transplant therapy may be actual transplantation of an organ/graft. Thus, the time period of "within 4 to 7 months post-transplant" is the same as the time period "within 4 to 7 months after exposure to transplant therapy". Accordingly, no subject matter has been disclaimed by this amendment, as it is solely formalistic.

Enablement Rejection

The Office has rejected claims 1-3, 8-11 and 15-18 as allegedly lacking enablement due to the use of the phrase "corresponding levels of expression". That phrase has been replaced with the phrase "the nucleic acid sequences set forth in SEQ ID NOs:29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, mRNA transcribed therefrom or protein encoded thereby" to clarify that the same set of nucleic acids, mRNAs or proteins should be measure in step a) as in step b) of the pending claims. Accordingly, no subject matter has been disclaimed, as this amendment is solely to clarify the instantly claimed subject matter.

The Office has rejected claims 1-3, 8-11 and 15-18 as allegedly lacking enablement due to recitation of SEQ ID NO: 36.[1] Specifically, the Office alleges that insufficient sequence data prevented Applicants' use of RT-PCR or Q-PCR to amplify W26469 (SEQ ID NO:36), and that

[1] The Office Action on page 7 mentions that the claims encompass detection of SEQ ID NOs:35 and 36, i.e., W26469 and AL049449. As in the previous response, Applicants note that Table 3 on page 21 clearly shows that AL049449 was identified by Q-PCR.

one of skill would not be able to use SEQ ID NO:36 to design primers or identify an encoded protein. That rejection is respectfully traversed.

Applicants detected the level of W26469 (SEQ ID NO:36) using microarray technology with RNA extracted from renal biopsies. Accordingly, at least this well know technique is readily available to identify the level of expression SEQ ID NO:36. Assuming, *arguendo*, that microarray technology was the only method currently available to measure the level of expression of SEQ ID NO:36, this fact would not render the claim non-enabled. According to MPEP 2164.08:

> The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling).

As for any enablement analysis, the key question relates to undue experimentation – in this case, whether undue experimentation would be required to identify which techniques for identifying the level of W26469 (SEQ ID NO:36) would be inoperative. It is the Office's contention that the specification teaches that Q-PCR was unavailable to identify W26469 (SEQ ID NO:36). Thus, no undue experimentation would be required to determine if Q-PCR technique is inoperative. The Office also contends that the EST entry for W26469 (provided by the Office) from GENEBANK® provides insufficient sequence information to determine a protein sequence. Thus, no undue experimentation would be required to determine if, e.g., antibody detection, is inoperative. The Office also contends that SEQ ID NO:36 provides insufficient sequence information to design primers specific for W26469. Thus, no undue experimentation would be required to determine if primer-based techniques are inoperative. Accordingly, if the Office is correct that only microarray technology is available to measure the level of expression of SEQ ID NO:36, the claims are surely enabled because "a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art." MPEP 2164.08.

However, Applicants submit that the Office need not resort to the above analysis regarding inoperative embodiments. The EST entry for W26469 (provided by the Office) from GENEBANK® provides all the guidance required to enable a skilled artisan to identify levels of W26469 using techniques other than microarray technology. Specifically, the EST entry for W26469 states:

1) The library used for sequencing the EST was a sub-library derived from a human retina cDNA library.

2) Inserts from the human retina cDNA library were isolated, randomly primed, PCR amplified, size-selected, and cloned into lambda gt10.

3) Individual plaques were arrayed and used as templates for PCR amplification, and these PCR products were used for sequencing.

The EST entry for W26469 from GENEBANK® also provides the sequences for the forward and backward primers, as well as the sequencing primer, that was used by Dr. Nathans of Johns Hopkins to identify the sequence of EST W26469.

Accordingly, an actual protocol for obtaining a clone for W26469 is provided by the EST entry for W26469 from GENEBANK®. Once a clone is obtained, it is routine experimentation to sequence said clone for providing RT- or Q-PCR primers, or to identify an open reading frame to obtain a protein sequence for the preparation of an antibody. Applicants respectfully submit that none of these traditional molecular biology techniques require undue experimentation, and that all are well within the capabilities of a skilled artisan. Indeed, the Federal Circuit has recently discussed the advancement of molecular biology methods, albeit in the context of obviousness, in *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009). In *Kubin*, the Court found a nucleotide sequence to be obvious because:

> [t]he record shows that the prior art teaches [the existence of] a protein of interest, a motivation to isolate the gene coding for that protein, and illustrative instructions to use a monoclonal antibody specific to the protein for cloning this gene.

Surely, if one of ordinary skill in the art could be lead to generate a specific nucleotide sequence by knowing the mere existence of a protein coupled with routine molecular biology and cloning techniques, then one of ordinary skill in the art would be similarly enabled to clone the gene related to the EST entry for W26469 from GENEBANK® (SEQ ID NO:36) and use that gene to design primers or to produce an antibody. For at least these reasons, Applicants respectfully submit that the claims are enabled.

Written Description Rejection

The Office's written description rejection finds basis, in part, on the use of the phrase "corresponding levels of expression". This phrase has been removed, rendering this aspect of the outstanding written description based rejection moot.

The Office's written description rejection finds basis, in part, on the use of SEQ ID NO:36 in the pending claims. For the following reasons, that rejection is respectfully traversed.

To satisfy the written description requirement, Applicants need only "reasonably convey" sufficient characteristics so that a skilled artisan can "visualize or recognize the identity" of the invention. *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985); *Regents of the University of California v. Eli Lilly, Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997). Applicants believe that the discussion in the enablement section above substantiates that Applicants were in possession of the claimed methods. More specifically, there is adequate evidence that Applicants possessed the claimed methods, and that a skilled artisan would recognize the same.

Applicants note that the Office states on pages 14-15 of the instant Office Action that SEQ ID NO:36 does not provided sufficient detail for one to envision the gene whose expression is predictive of chronic allograft rejection. However, Applicants' claims are not product claims. Thus, Applicants are not required to provide detail to allow a skilled artisan to envision the gene related to the EST entry for W26469 (SEQ ID NO:36). Applicants' claims are method claims that use expression information related to various sequences, including SEQ ID NO:36, to diagnose and monitor CR. A skilled artisan does not need to know the detailed structure of SEQ ID NO:36 to perform these methods, and a skilled artisan would recognize that Applicants possessed these methods without providing such detail. To satisfy the written description requirement, Applicants need only provide enough detail such that, when that detail is coupled with the knowledge available to one of ordinary skill in the art, a skilled artisan would understand that at the time of filing the instant Application, Applicants possessed what they now claim. For at least these reasons, Applicants respectfully submit that the claims are adequately described.

CONCLUSION

In light of the above amendments, observations and remarks, Applicants respectfully submit that the presently claimed invention satisfies 35 U.S.C. §112, and is neither disclosed nor suggested by any art of record. Accordingly, reconsideration and allowance of all claims in this application is earnestly solicited.

Applicants' undersigned attorney may be reached in our New Jersey office by telephone at (862) 778-9308. All correspondence should continue to be directed to our below-listed address.

Respectfully submitted,

Leslie Fischer
Attorney for Applicants
Reg. No. 58,393

Novartis Pharmaceuticals Corp.
Patents Pharma
One Health Plaza, Building 104
East Hanover, NJ 07936-1080
(862) 778-9308

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